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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/288,837	04/08/1999	GENE H. MACDONALD	5470-238	7924
20792	7590	03/09/2004	EXAMINER	
MYERS BIGEL SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627			LUCAS, ZACHARIAH	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/288,837

Applicant(s)

MACDONALD ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 84, 89-93, 95, 97-104, 109 and 114 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 84, 89-93, 95, 97-104, 109 and 114 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date 3-5-04
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 84, 89-93, 95, 97-104, 109, and 114 are pending and under consideration. Claims 84, 85, 89-93, and 95-114 were pending and rejected in the prior action, mailed on July 2, 2003. In the After Final Response submitted after the prior action, the Applicant argued that the prior action should not be a Final Action; cancelled claims 85, 96, 105-108, and 110-113; and amended claims 84, 91, 92, 95, 100, 101, 103, 104, 109, and 114.
2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claim Rejections - 35 USC § 102

3. **(Prior Rejection- Withdrawn)** Claims 105, 106, 109, 110, 111, and 114 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,843,723, issued to Dubensky et al. Because the Office finds that this reference is more appropriately applied under 35 U.S.C. 103(a), the anticipation rejection over Dubensky is withdrawn.

Claim Rejections - 35 USC § 103

4. **(Prior Rejection- Restated and Maintained)** Claims 84, 90-93, and 95-114 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over either 1) Johnston et al., WO 95/32733 or 2) U.S. Patent Number 5,843,723, issued to Dubensky et al. in view of U.S. Patent 5,792,462, issued to Johnston et al. (Johnston 2), with either 1 or 2 further in view of

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Falo et al., U.S. Patent Number 5,951,975. In that action it was stated that although the Applicant had persuasively argued the distinction between the use of the method of Falo and that of the present invention. The rejection was maintained in view of the teachings of the Dubensky reference, which teaches the use alphavirus replicons to deliver antigens, and which suggests the use of the particles for the delivery of cancer antigens. AT present, the rejection is being maintained to the extent that the claims read on compositions of either alphavirus replicons generally, or the use of the VEE replicons that encode other than the neu antigen used in the example described in the supplemental Olmsted declaration. The rejection is also restated to include claim 89. Although this claim was not listed as rejected in the prior action, claim 90, which depends from claim 89, and claim 98, which described similar subject matter, were both rejected. Thus, the addition of claim 90 to the list of rejected claims is not deemed to affect the scope of the rejected subject matter or to add new issues to the rejection. In accordance with the above, and with the fact that Falo is no longer relied upon, the rejection is restated as a rejection of claims 84, 89-93, 95, 97-104, 109, and 114 over the teachings of Dubensky in view of Johnston 1 and 2.

It is noted that, in the prior action, the Applicant was indicated as having distinguished between the replicon particles of Dubensky and those of the present application. In specific, the applicants argued a distinction between the particles of Dubensky and the present application. The Applicant described Dubensky as teaching alphavirus particles which lack the genes encoding the structural proteins, thus rendering the particles unable to propagate; whereas the claims identified above use attenuated viruses, which are able to replicate, but at reduced levels. See, page 11 of the Feb 2003 response. Thus, based on previous arguments by the Applicant, the

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claims were read in such a manner that Dubensky was not considered to teach the replicons of the claimed inventions. The obviousness rejection thus relied on the teachings of Johnston to teach the additional changes to the replicon particle such that they fell within the claimed language.

However, in the form of the Caley Declaration, the Applicants submitted evidence (and argued on page 12 of the After Final Response) that "replicon particles are capable of one round of infection; they cannot spread (i.e. infect) other cells." Thus, the Applicant has contradicted their earlier arguments in the Declaration, and now indicates that the claimed replicon particles with attenuating mutations are in fact incapable of more than one round of infection. By doing so, the Applicant has in effect changed the scope of the claimed invention such that the claims now read on the Dubensky replicon particles. Thus, while the Examiner agrees with the Applicant's assertion on page 14 of the After Final Response that there had previously been an understanding as to the association between the Dubensky particles and those of the present invention, such is no longer the case.

The Applicant traverses the present rejection on the grounds that there would have been no reasonable expectation of success in the combination, and that the present invention provided unexpected results over what may have been expected by using the particles suggested by the indicated references. It is first noted that, while the Applicant has established the distinction between the antigens of Falo and of the present invention, as indicated by the prior action, the Applicant has not provided such a distinction between the cancer antigens suggested by Dubensky and those of the present invention. Thus, the Applicant's arguments with reference to Falo are not found persuasive. Further, in that Dubensky explicitly indicates that the described

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replicon particles would be effective in anticancer treatments, those in the art would have had a reasonable expectation of success in the use of the vectors.

The Applicant further challenges the finding of a reasonable expectation of success on the grounds of the teachings of Weiner. The Applicant argues that, based on the teachings of Weiner, which teaches disadvantages of viral vectors, those in the art would not have considered alphavirus vectors for use in the delivery of cancer antigens. This argument is not found persuasive. First, the reference does not teach that alphavirus specifically, or viral vectors in general, do not work. The patent merely teaches several disadvantages of the use of such vectors that are not encountered in the use of the DNA vaccines disclosed in that patent. In short, Weiner purports to teach an improved method of DNA vaccination that the use of viral vectors. However, the development of new inventions to perform the same or similar function does not make older technology any less obvious to those of ordinary skill in the art, and does not teach away from the prior invention in the sense of rebutting the motivational element of establishing obviousness. See e.g. In re Gurley, 31 U.S.P.Q. 2d 1130, 1131-1132 (Fed. Cir. 1994). The Federal Circuit stated in Gurley that a "known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *Id.*, at 1132. In short, the court held that teaching a better solution to problem is not a teaching away from a previously known, and operable, solution.

Further, the art teaches that the use of alphavirus replicons, due to characteristics peculiar to these viruses, allow them to be particularly effective in the induction of immune responses. See, e.g. Pushko et al., *Virology* 239: 389-401 (of record in the Jan 2000 IDS- teaching the high level expression of proteins by alphavirus replicon particles). This is particularly true when the

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alphavirus is the VEE vector. See, Caley et al., J Virol 71(4): 3031-3038, at pages 3031-32 (teaching that the lymphotropic nature of the VEE replicon makes the particle particularly attractive as a antigen vector). Thus, the art provides adequate support for the conclusions drawn from the Dubensky reference that the alphavirus particles would be effective vectors for the induction of immune responses against cancer antigens. It is noted that these references teach that the VEE vectors have all of the characteristics pointed out by Caley in the Declaration.

The Applicant further argues that the claimed invention is not obvious over the teachings of the art in that the Applicant has demonstrated unexpected results in the use of the claimed replicons in anticancer therapy. As indicated in the Olmsted Declarations, the Applicant does appear to have demonstrated that the use of the present replicons has achieved unexpected results (as the high efficacy of the viral vector at inducing a protective response). However, these results are limited to the use of the VEE vector. The teachings in the Declarations of Dr. Olmstead, submitted in June 2001 and April 2003; the Long reference cited in the February 2003 response; and the Gardner and Velders references cited in the After Final Response each discuss the use of VEE replicon vectors. These references therefore thus provide no basis for those in the art to expect that any viral replicon vector would be equally efficacious. Nor has the Applicant provided any evidence that the unexpected results achieved using the VEE replicons would be also be achieved using any alphavirus replicon vector.

In addition to the failure of the Applicant to demonstrate the unexpected results would be likely to result from the use of any alphavirus particles, the art also provides reasons why such results may be limited to the VEE replicon vector. For example, the Caley reference teaches that "unlike other alphaviruses, VEE is lymphotropic," and that this characteristic of the virus

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“confers the ability to specifically target the expression of heterologous protein to lymphoid tissues, where one might expect the initiation of a vigorous immune response.” Caley, pages 3031-32. See also, Gardner et al., J Virol 74(24): 11849-57 (reaffirming that other alphavirus are not lymphotropic, but that the Sindbis virus may be made so through protein mutagenesis). Thus, the art provides further reasons to suspect that the improved results achieved by using the VEE vector would not be common to alphavirus replicon vectors in general without further teachings to those provided in the current application.

However, because the Applicant has demonstrated unexpected results in the model described in the Olmsted supplemental reference, the rejection is withdrawn to the extent of the replicon vector described therein (I.e. the VEE replicon encoding the neu (Her2) antigen). However, as the Applicant has not established that such results would also be found using any antigen, the rejection is maintained for the reasons above and for the reasons of record.

5. **(Prior Rejection- Withdrawn)** Claims 84, 85, 90-93, and 95-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiner et al., U.S. Patent 6,468,982, in view of the Johnston references. Because the combination of these references alone do not teach or suggest the use of viral vectors for the induction of anti-cancer immune responses, the rejection is withdrawn.

Conclusion

6. No claims are allowed.

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7. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Disis et al., J Immunol, 156 : 3151-58 (1996). This reference teaches that immune responses may be induced against the self-tumor antigen HER-2/neu. Further, the reference indicates that certain peptides of the antigen are better able to induce such a response than is the full neu antigen. The reference teaches that, although an immune response could not be induced in rats against the complete rat neu antigen, responses could be induced against epitope found within the protein. The reference does not teach or suggest the use of DNA vaccines or viral vectors.

8. **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

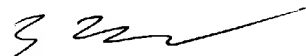
Application/Control Number: 09/288,837

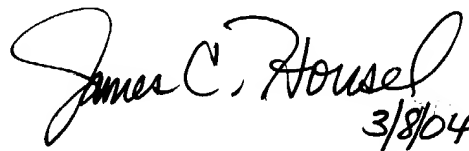
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Z. Lucas
Patent Examiner
March 5, 2004


3/8/04

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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